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NEWS	8	Mar 22	TRCTHERMO no longer available
NEWS	9	Mar 28	US Provisional Priorities searched with P in CA/CAplus and USPATFULL
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NEWS	17	Apr 22	BIOSIS Gene Names now available in TOXCENTER
NEWS	18	Apr 22	Federal Research in Progress (FEDRIP) now available
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NEWS	21	Jun 10	PCTFULL has been reloaded
NEWS	22	Jul 02	FOREGE no longer contains STANDARDS file segment

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=> s IgE
L1       108894 IGE

=> s l1 and cannine
L2            0 L1 AND CANNINE

=> s l1 and canine
L3          494 L1 AND CANINE

=> s l3 and CH3
L4            1 L3 AND CH3

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L4   ANSWER 1 OF 1  SCISEARCH  COPYRIGHT 2002 ISI (R)
2000:407589   The Genuine Article (R) Number: 317PX. Multiple roles for the
     major histocompatibility complex class I-related receptor FcRn.  Ghetie V
     (Reprint); Ward E S. UNIV TEXAS, SW MED CTR, CTR IMMUNOL, 5323 HARRY HINES
     BLVD, DALLAS, TX 75235 (Reprint); UNIV TEXAS, SW MED CTR, CTR CANC
     IMMUNOBIOL, DALLAS, TX 75235. ANNUAL REVIEW OF IMMUNOLOGY (JUL 2000) Vol.
     18, pp. 739-766. Publisher: ANNUAL REVIEWS. 4139 EL CAMINO WAY, PO BOX
     10139, PALO ALTO, CA 94303-0139. ISSN: 0732-0582. Pub. country: USA.
     Language: English.
     *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB       Multiple functions have recently been identified for the neonatal Fc
     receptor FcRn. In addition, a human homolog of the rodent forms of FcRn
     has been identified and characterized. This major histocompatibility
     complex class I-related receptor plays a role in the passive delivery of
     immunoglobulin (Ig)Gs from mother to young and the regulation of serum IgG
     levels. In addition, FcRn expression in tissues such as liver, mammary
     gland, and adult intestine suggests that it may modulate IgG transport at
     these sites. These diverse functions are apparently brought about by the
     ability of FcRn to bind IgGs and transport them within and across cells.
     However, the molecular details as to how FcRn traffics within cells have
     yet to be fully understood, although in vitro systems have been developed
     for this purpose. The molecular nature of the FcRn-IgG interaction has
     been studied extensively and encompasses residues located at the CH2-
     CH3 domain interface of the Fc region of IgG. These Fc amino acids
     are highly conserved in rodents and man and interact with residues
     primarily located on the alpha 2 domain of FcRn. Thus, it is now possible
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to engineer IgGs with altered affinities for FcRn, and this has relevance to the modulation of **Ige** serum half-lift and maternofetal IgG transport for therapeutic applications.

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=> s l3 and CH4
L5            0 L3 AND CH4

=> s l3 and fusion
L6           19 L3 AND FUSION

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PROCESSING COMPLETED FOR L6
L7             6 DUP REMOVE L6 (13 DUPLICATES REMOVED)

=> d l7 1-6 cbib abs
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L7 ANSWER 1 OF 6 MEDLINE DUPLICATE 1
2001558505 Document Number: 21491203. PubMed ID: 11604166. Recombinant **canine** IL-13 receptor alpha2-Fc **fusion** protein inhibits **canine** allergen-specific-**IgE** production in vitro by peripheral blood mononuclear cells from allergic dogs. Tang L; Boroughs K L; Morales T; Stedman K; Sellins K; Clarke K; McDermott M; Yang S; McCall C. (Heska Corporation, 1613 Prospect Parkway, Fort Collins, CO 80525, USA.. tangl@heska.com) . VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (2001 Nov) 83 (1-2) 115-22. Journal code: 8002006. ISSN: 0165-2427. Pub. country: Netherlands. Language: English.

AB Human IL-13, like IL-4, is involved in the regulation of B-cell development, **IgE** synthesis and allergic responses. However, because IL-13 does not affect either murine Ig class switching or **IgE** production in vitro, the use of murine models to study the role of IL-13 in **IgE**-mediated diseases has been limited. In this communication, we report that recombinant protein of **canine** IL-13 (rcaIL-13) stimulates production of allergen-specific-**IgE** in vitro by peripheral blood mononuclear cells (PBMC) from flea allergen-sensitized dogs, and that this stimulation activity is specifically inhibited by recombinant protein of **canine** IL-13Ralpha2 and Fc fragment of **canine** IgG heavy chain (rcaIL-13Ralpha2-Fc). The data suggest that the regulatory effects of IL-13 on **IgE** production in **canine** PBMC are similar to those reported in humans. Thus, **canine** IL-13 may be a central mediator of allergic diseases in dogs, and allergic dogs may be excellent models for research on **IgE**-mediated diseases in humans.

L7 ANSWER 2 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
2001:175320 Document No.: PREV200100175320. Soluble **canine** IL-13 receptor alpha2-Fc **fusion** protein inhibits **canine** allergen-specific-**IgE** production stimulated by IL-13 in vitro. Tang, Liang (1); Boroughs, Karen (1); Stedman, Kim E. (1); Sellins, Karen (1); Morales, Tony (1); McDermott, Martin (1); Yang, Shumin (1); McCall, Catherine A. (1). (1) Heska Corporation, Fort Collins, CO USA. Journal of Allergy and Clinical Immunology, (February, 2001) Vol. 107, No. 2, pp. S91. print. Meeting Info.: 57th Annual Meeting of the American Academy of Allergy, Asthma and Immunology New Orleans, Louisiana, USA March 16-21, 2001 ISSN: 0091-6749. Language: English. Summary Language: English.

L7 ANSWER 3 OF 6 MEDLINE
2001060249 Document Number: 20528604. PubMed ID: 11074254. Identification, cloning, and characterization of a major cat flea salivary allergen (Cte f 1). McDermott M J; Weber E; Hunter S; Stedman K E; Best E; Frank G R; Wang R; Escudero J; Kuner J; McCall C. (Heska Corporation, 1613 Prospect Parkway, Fort Collins, CO 80525, USA.. mcdermm@heska.com) . MOLECULAR IMMUNOLOGY, (2000 May) 37 (7) 361-75. Journal code: 7905289.

ISSN: 0161-5890. Pub. country: ENGLAND: United Kingdom. Language: English.

AB An 18 kDa protein isolated from saliva of the cat flea, Ctenocephalides felis, elicits a positive intradermal skin test (IDST) in 100 and 80% of experimental and clinical flea allergic dogs, respectively. Using solid-phase enzyme-linked immuno assay (ELISA), this protein detected **IgE** in 100 and 80% of experimental and clinical flea allergic dogs, respectively. A cDNA (pFSI) encoding a full-length Cte f 1 protein was isolated from a C. felis salivary gland cDNA library, using a combination of PCR and hybridization screening. This cDNA is 658 bp in length, and contains an open reading frame of 528 bp. The open reading frame encodes a protein of 176 amino acids, consisting of an 18 amino acid signal sequence and a 158 amino acid mature protein. The calculated molecular weight and pI of the mature protein are 18106 Da and 9.3, respectively. The protein, named Cte f 1, is the first novel major allergen described for **canine** flea allergy. Recombinant Cte f 1 (rCte f 1) was expressed in Escherichia coli, Pichia pastoris and baculovirus infected Trichoplusia ni cells. Approximately, 90% of the rCte f 1 expressed in E. coli accumulated in insoluble inclusion bodies, which could be refolded to a soluble mixture of disulfide isomers with partial **IgE** binding activity. Small quantities of an apparently correctly refolded form of rCte f 1, which had **IgE** binding activity equal to the native antigen, was isolated from the soluble fraction of E. coli cells. However, P. pastoris and baculovirus infected insect cells expressed and secreted a fully processed, correctly refolded and fully active form of rCte f 1. Mass spectrometry analysis of the active forms of rCte f 1confirmed that eight intact disulfide bonds were present, matching the number observed in the native allergen. The relative ability of rCte f 1 to bind **IgE** in the serum of flea allergic animals, produced in these three expression systems, matched that of the native allergen. Competition ELISA demonstrated that approximately 90% of the specific **IgE** binding to native Cte f 1 could be blocked by the different forms of rCte f 1.

L7 ANSWER 4 OF 6 MEDLINE DUPLICATE 3

2000407793 Document Number: 20349799. PubMed ID: 10889305. In vitro **IgE** but not IgG production of **canine** peripheral blood B cells is inhibited by CD40 ligation. Goedert S; Schiessl B; Zunic M; Schiebl C; Mayer P; de Weck A L; Liehl E; Mudde G C. (Allergy Section, Department of Immuno-Dermatology, Novartis Research Institute, Brunnerstr. 59, A-1235, Vienna, Austria.. goedert@mpiib-berln.mpg.de) . VETERINARY IMMUNOLOGY AND IMMUNOPATHOLOGY, (2000 Jun 30) 75 (1-2) 135-49. Journal code: 8002006. ISSN: 0165-2427. Pub. country: Netherlands. Language: English.

AB The aim of this study was to investigate in vitro **IgE** induction in peripheral **canine** B cells. CD21(+) B cells were purified from the peripheral blood of beagle dogs by positive selection via magnetic separation to a purity of >/=95%. Subsequently, proliferation, and IgG and **IgE** production of **canine** B cells were investigated after stimulation with human recombinant Interleukin-4 (hrIL-4) and human recombinant Interleukin-2 (hrIL-2) in the presence or absence of CD40L-CD8 **fusion** protein (CD40L) of mouse origin. We could demonstrate that **canine** B cells react on hrIL-2 alone by proliferation and IgG production but not by **IgE** secretion, whereas activation with hrIL-4 induced proliferation and mainly **IgE** production. Together, both cytokines synergistically increased B cell proliferation as well as IgG and **IgE** production. We could also show that mouse CD40L induces proliferation of dog B cells, which is further enhanced by addition of hrIL-4. Unexpectedly, CD40L led to a dramatic decrease in the IL-4 mediated **IgE** secretion (82% inhibition on an average). In contrast, IgG production was not affected significantly by CD40L. The same effects of CD40L were observed when B cells were stimulated by a combination of IL-2 and IL-4 and this inhibition could not be abrogated by increasing the amounts of IL-4. In summary, activation of **canine**

B cells from peripheral blood by hrIL-4 in the presence or absence of hrIL-2 led to marked **IgE** production that is strongly and in a dose-dependent manner inhibited by CD40L. Stimulation of IgG production is not influenced by CD40L.

L7 ANSWER 5 OF 6 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
2000:140257 Document No.: PREV200000140257. Detection of allergen-specific **IgE** using a FcepsilonRIalpha/luciferase **fusion** protein. Weber, E. R. (1); McDermott, M. J. (1); Morales, T. H. (1); Snyder, S. E. (1); Miller, J. L. (1); Jensen, W. A. (1). (1) Heska Corporation, Fort Collins, CO USA. Journal of Allergy and Clinical Immunology., (Jan., 2000) Vol. 105, No. 1 part 2, pp. S114-S115. Meeting Info.: 56th Annual Meeting of the American Academy of Allergy, Asthma and Immunology. San Diego, California, USA March 03-08, 2000 American Academy of Allergy, Asthma and Immunology. ISSN: 0091-6749. Language: English. Summary Language: English.

L7 ANSWER 6 OF 6 MEDLINE DUPLICATE 4
96005834 Document Number: 96005834. PubMed ID: 7558131. **Canine** **IgE** monoclonal antibody specific for a filarial antigen: production by a **canine** x murine heterohybridoma using B cells from a clinically affected lymph node. Gebhard D; Orton S; Edmiston D; Nakagaki K; DeBoer D; Hammerberg B. (College of Veterinary Medicine, North Carolina State University, Raleigh, USA.) IMMUNOLOGY, (1995 Jul) 85 (3) 429-34. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.
AB **Canine** popliteal lymph node cells taken at the onset of clinical disease from a rear limb infected with the filarial nematode Brugia pahangi were fused with mouse myeloma cell line P3X63.Ag8.653 cells. Of the several **canine** immunoglobulin-producing clones from this **fusion**, one was found to produce **canine IgE** specific for a filarial nematode antigen. The cell line has undergone limiting dilution cloning six times over the past 3 years and continues to produce monoclonal antibody of the **IgE** subclass at a rate of greater than 3 mg/l. Sodium dodecyl sulphate-polyacrylamide gel electrophoresis (SDS-PAGE) of the cell culture supernatant protein that bound to protein A beads, showed bands at molecular weights (MW) of approximately 75,000 and 25,000 that were characteristic of epsilon and kappa or lambda chains, respectively. A mouse monoclonal antibody specific for **canine IgE** bound the 75,000 MW band, as demonstrated by Western blot. Western blots of aqueous extracts of adult filarial nematodes demonstrated binding of the **canine** **IgE** monoclonal antibody to a single 35,000 MW peptide from B. pahangi but not Dirofilaria immitis; immunochemistry using frozen sections of adult worms, microfilariae and fourth stage larvae revealed focal binding of the monoclonal **IgE** to worm tissue adjacent to dorsal and ventral cords of only Brugia adults.

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L8        5767 (MORSEY M?/AU OR SHEPPARD M?/AU OR WHEELER D?/AU)

=> s l8 and IgE
L9          23 L8 AND IGE

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PROCESSING COMPLETED FOR L9
L10          7 DUP REMOVE L9 (16 DUPLICATES REMOVED)

=> d l10 1-7 cbib abs
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L10 ANSWER 1 OF 7 CAPLUS COPYRIGHT 2002 ACS
2002:272796 Document No. 136:293510 Anti-allergic vaccines comprising peptides of Fc portion of **IgE** .epsilon. heavy chain and carrier

protein. **Morsey, Mohamad Ali; Sheppard, Michael George ; Wheeler, David Walter** (Pfizer Products Inc., USA). Eur. Pat. Appl. EP 1195161 A2 20020410, 38 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 2001-307247 20010824. PRIORITY: US 2000-PV228989 20000830.

AB The present invention provides compns. and methods for the use of antigenic peptides derived from the Fc portion of the epsilon heavy chain of an **IgE** mol. as vaccines for the treatment and prevention of **IgE**-mediated allergic disorders. In particular, the invention provides compns., methods for the treatment and prevention of **IgE** -mediated allergic disorders comprising an immunogenic amt. of one or more antigenic peptides derived from the CH3 domain or junction of Ch-3/CH4 domain of an **IgE** mol. and methods for the evaluation of **IgE** mediated allergies in dogs. The allergic disorder is asthma, allergic rhinitis, gastrointestinal allergy, food allergy, eosinophilia, conjunctivitis, or glomerular nephritis. The vaccine compns. may also comprises carrier protein such as KLH, PhoE, rmLT, TraT and gD from BhV-1 virus; and adjuvant such as aluminum hydroxide, monophosphoryl lipid A, Thr-MDP, immunostimulatory oligonucleotide, cytokine, interleukin 12, interleukin 2, interleukin 1, saponin, cholera toxin, heat labile toxin, etc.

L10 ANSWER 2 OF 7 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.

2001:83036 Document No.: PREV200100083036. Effect of cytokines on **IgE** switching by human B cells. Bitsaktsis, Con. (1); **Wheeler, D. (1)** ; Kemeny, D. M. (1). (1) Dept. Immunology, Rayne Institute, 123 Coldharbour Lane, London, SE5-9NU UK. Immunology, (December, 2000) Vol. 101, No. Supplement 1, pp. 79. print. Meeting Info.: Annual Congress of the British Society for Immunology Harrogate, UK December 05-08, 2000 British Society for Immunology. ISSN: 0019-2805. Language: English. Summary Language: English.

L10 ANSWER 3 OF 7 SCISEARCH COPYRIGHT 2002 ISI (R)

1999:617501 The Genuine Article (R) Number: 223EE. Heligmosomoides polygyrus immunomodulatory factor (IMF), targets T-lymphocytes. Telford G (Reprint); **Wheeler D J;** Appleby P; Bowen J G; Pritchard D I. KNOLL PHARMACEUT, RES DEPT R3, PENNYFOOT ST, NOTTINGHAM NG1 1GF, ENGLAND (Reprint); RHONE POULENC RORER, DAGENHAM RM10 7XS, ESSEX, ENGLAND; UNIV NOTTINGHAM, DEPT LIFE SCI, NOTTINGHAM NG7 2RD, ENGLAND. PARASITE IMMUNOLOGY (DEC 1998) Vol. 20, No. 12, pp. 601-611. Publisher: BLACKWELL SCIENCE LTD. P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND. ISSN: 0141-9838. Pub. country: ENGLAND. Language: English.
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Experiments were performed to investigate the immunological site of action of an immunomodulatory factor (IMF), isolated from the gastrointestinal nematode Heligmosomoides polygyrus. IMF inhibited antibody production in murine and human 'T-helper (Th-2) driven' immunoassays. The effects were mediated via T lymphocytes as T cell-depleted cultures Sailed to respond to IMF, a result confirmed by repulsing discrete cell subsets with the immunomodulant. Although the molecular nature and mode of action of IMF has yet to be determined it would appear to be a relatively small nonproteinaceous molecule. From this data, we suggest that H. polygyrus secretes a systemically-active IMF from the intestinal lumen, to down-regulate Th-2 cell development ill order to promote its survival in a potentially immunologically hostile environment.

L10 ANSWER 4 OF 7 MEDLINE DUPLICATE 1

1999069260 Document Number: 99069260. PubMed ID: 9767464. Inhibition of sCD23 and immunoglobulin E release from human B cells by a metalloproteinase inhibitor, GI 129471. **Wheeler D J;** Parveen S; Pollock K; Williams R J. (Department of Cell Biology, Rhone-Poulenc-Rorer Ltd, Dagenham Research Centre, Dagenham, Essex, UK.) IMMUNOLOGY, (1998

Sep) 95 (1) 105-10. Journal code: 0374672. ISSN: 0019-2805. Pub. country: ENGLAND: United Kingdom. Language: English.

AB Soluble CD23 (sCD23) has been proposed to play an important role in the up-regulation of immunoglobulin E (**IgE**) synthesis. Production of sCD23 is dependent on the proteolytic cleavage of membrane CD23, but the protease(s) involved in this process remain unknown. Preliminary data, obtained by testing a panel of protease inhibitors, suggested that this enzyme may be a zinc-dependent metalloproteinase. Therefore, we investigated the effect of a standard hydroxamate-type Zn2+ metalloproteinase inhibitor (GI 129471) on both sCD23 and **IgE** release from human tonsillar B cells, stimulated with interleukin-4 (IL-4) and anti-CD40. Incubation of cells for 3 days with GI 129471 inhibited the production of sCD23 with an IC50 of 602 nm+/-3 nm (n=3), but by 14 days the activity of the compound against sCD23 had decreased by greater than threefold (IC50 2+/-0.26 microM; n=3). On the other hand, GI 129471 caused a potent inhibition of **IgE** production, with no apparent loss of activity over the culture period (14 days: IC50 250 nm+/-72 nm; n=3). Time-course studies showed that, despite loss of activity against sCD23, inhibition of sCD23 production early in the culture was able to cause a potent and long-lasting inhibitory effect on **IgE**. Furthermore, we also showed that the activity of GI 129471 is selective for **IgE**, as no effect was seen on immunoglobulin G1 (IgG1) or IgG4 production at test concentrations as high as 10 microM. These results support the hypothesis that metalloproteinases may be involved in the proteolytic cleavage of CD23 and subsequent regulation of **IgE** synthesis. Inhibition of the protease(s) responsible for such cleavage may be of value in the treatment of allergic disease.

L10 ANSWER 5 OF 7 MEDLINE DUPLICATE 2

1998084452 Document Number: 98084452. PubMed ID: 9423836. The Pseudomonas aeruginosa quorum-sensing signal molecule N-(3-oxododecanoyl)-L-homoserine lactone has immunomodulatory activity. Telford G; **Wheeler D**; Williams P; Tomkins P T; Appleby P; Sewell H; Stewart G S; Bycroft B W; Pritchard D I. (Department of Life Science, University of Nottingham, University Park, United Kingdom.) INFECTION AND IMMUNITY, (1998 Jan) 66 (1) 36-42. Journal code: 0246127. ISSN: 0019-9567. Pub. country: United States. Language: English.

AB Diverse gram-negative bacterial cells communicate with each other by using diffusible N-acyl homoserine lactone (AHL) signal molecules to coordinate gene expression with cell population density. Accumulation of AHLs above a threshold concentration renders the population "quorate," and the appropriate target gene is activated. In pathogenic bacteria, such as Pseudomonas aeruginosa, AHL-mediated quorum sensing is involved in the regulation of multiple virulence determinants. We therefore sought to determine whether the immune system is capable of responding to these bacterial signal molecules. Consequently the immunomodulatory properties of the AHLs N-(3-oxododecanoyl)-L-homoserine lactone (OdDHL) and N-(3-oxohexanoyl)-L-homoserine lactone (OHHL) were evaluated in murine and human leukocyte immunoassays in vitro. OdDHL, but not OHHL, inhibited lymphocyte proliferation and tumor necrosis factor alpha production by lipopolysaccharide-stimulated macrophages. Furthermore, OdDHL simultaneously and potently down-regulated the production of IL-12, a Th-1-supportive cytokine. At high concentrations (>7 x 10(-5) M) OdDHL inhibited antibody production by keyhole limpet hemocyanin-stimulated spleen cells, but at lower concentrations (<7 x 10(-5) M), antibody production was stimulated, apparently by increasing the proportion of the immunoglobulin G1 (IgG1) isotype. OdDHL also promoted **IgE** production by interleukin-4-stimulated human peripheral blood mononuclear cells. These data indicate that OdDHL may influence the Th-1-Th-2 balance in the infected host and suggest that, in addition to regulating the expression of virulence determinants, OdDHL may contribute to the pathogenesis of P. aeruginosa infections by functioning as a virulence determinant per se.

L10 ANSWER 6 OF 7 MEDLINE DUPLICATE 3
96381527 Document Number: 96381527. PubMed ID: 8789540. Peripheral blood based T cell-containing and T cell-depleted culture systems for human **IgE** synthesis: the role of T cells. **Wheeler D J;** Robins R A; Pritchard D I; Bundick R V; Shakib F. (Department of Immunology, University of Nottingham, UK.) CLINICAL AND EXPERIMENTAL ALLERGY, (1996 Jan) 26 (1) 28-35. Journal code: 8906443. ISSN: 0954-7894. Pub. country: ENGLAND: United Kingdom. Language: English.

AB BACKGROUND: Comparable T cell-containing and T cell-depleted culture systems for human **IgE** synthesis are currently not available. OBJECTIVE: This has prompted us to develop peripheral blood mononuclear cell (PBMC) based culture systems for human **IgE** synthesis in the presence and absence of T cells. METHODS: In this paper we describe simplified conditions for in vitro synthesis of high levels of **IgE** by human peripheral blood B cells, both in T cell-containing cultures and in anti-CD40 stimulated T cell-depleted cultures. RESULTS: T cell-depleted cultures released approximately 20 times more **IgE** [range 410-2220 ng/mliter (mean 1270 ng/mliter); based on six experiments using cells from three donors] than did T cell-containing cultures [range 23-105 ng/mliter (mean 58 ng/mliter); based on 15 experiments using cells from three donors]. Reconstitution experiments were performed to investigate the role of T cells on **IgE** synthesis. Adding T cells back to the anti-CD40 stimulated T cell-depleted cultures resulted in a dose-dependent inhibition of **IgE** production. In the absence of anti-CD40 low numbers of T cells stimulated, while high numbers suppressed, **IgE** production: the optimal ratio of T cells to non-T cells for maximal **IgE** production was found to be 1:1. At this ratio, irradiated (non-replicating) T cells supported a much greater **IgE** synthesis than did non-irradiated T cells. CONCLUSION: The development of these systems provides directly comparable T cell-containing and T cell-depleted cultures for human **IgE** synthesis from peripheral blood, allowing further study of the role of T cells in **IgE** regulation. These systems will also be of use for determining whether potential modulators of **IgE** synthesis act on the T cells or on other cell types.

L10 ANSWER 7 OF 7 MEDLINE DUPLICATE 4
96003955 Document Number: 96003955. PubMed ID: 7554405. Potentiation of in vitro synthesis of human **IgE** by cyclosporin A (CsA). **Wheeler D J;** Robins A; Pritchard D I; Bundick R V; Shakib F. (Division of Molecular and Clinical Immunology, University of Nottingham, Medical School, UK.) CLINICAL AND EXPERIMENTAL IMMUNOLOGY, (1995 Oct) 102 (1) 85-90. Journal code: 0057202. ISSN: 0009-9104. Pub. country: ENGLAND: United Kingdom. Language: English.

AB In this study, we investigated the modulatory effects of CsA on in vitro synthesis of **IgE**, IgG1 and IgG4 by human peripheral blood mononuclear cells (PBMC). In contrast to its known immunosuppressive effect, we have demonstrated that a low dose of CsA (10(-7) M, 120 ng/ml) potentiated **IgE** production by up to 40-fold (i.e. from 33 +/- 4.5 to 1346 +/- 290 ng/ml). This potentiation was specific for **IgE** since no such effect was demonstrable with IgG1 and IgG4. Potentiation of **IgE** synthesis by CsA in the PBMC cultures was partly due to CsA acting on T cells, as demonstrated by the addition of CsA-treated T cells to T cell-depleted cultures. However, potentiation was also demonstrable in a T cell-depleted, anti-CD40-stimulated culture (four-fold increase from 400 +/- 48 to 1606 +/- 127 ng/ml). Our data therefore suggest that there are at least two mechanisms for CsA-induced potentiation of **IgE** synthesis, one T cell-dependent and the other T cell-independent. The clinical implications of these findings are discussed with regard to the use of CsA in the treatment of Th2-mediated diseases.

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